REMARKS

Claims 1-11 were pending in the subject application. Applicants have amended claims 1, 4 and 11 to clarify the claimed subject matter. Applicants have also added claims 12 and 13, which find support, *inter alia*, on page 62, lines 12-13 and page 34, lines 1-7 of the originally-filed specification. Applicants respectfully request entry of this amendment such that claims 1-13 will be pending.

Specification

The Examiner objects to the phrase "Pemphigus vulgaris" alleging that (a) it should not be italicized and that (b) "Pemphigus" should not be capitalized unless it is the first word of a sentence. The Examiner further requests that the term "in vitro" be italicized and that applicants correct additional typographical errors of which they are aware.

In response, applicants have amended the specification as requested by the Examiner and have corrected other typographical errors, thereby obviating this ground of rejection. Due to the number of amendments to the specification, applicants are submitting a substitute specification without the claims, as a marked-up version and a clean version, Exhibits A and B respectively, in accordance with 37 CFR 1.125. Further, as required by 37CFR 1.125(b), applicants submit that the substitute specification includes no new matter. Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Oath/Declaration

The Examiner objects to the declaration as allegedly failing to comply with 37 CFR 1.67(a). Specifically, the Examiner alleges (a) that the declaration fails to identify the application by its serial number and (b) that it contains an alteration (to the address of one inventor) that is not initialed and dated.

In response, applicants submit a newly executed declaration correcting these alleged deficiencies. Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Claim Rejections under 35 USC 112 1st Paragraph-Enablement

The Office Action rejects claims 1-11 under 35 USC 112 1st paragraph as allegedly failing to comply with the enablement requirement. The arguments set forth in the Office Action will be addressed below in the order in which they appeared.

(a) The Office Action alleges that the phrase "consisting essentially of" as recited in claim 1 is not enabled by the specification; the Office Action further alleges that according to the specification, this phrase encompasses the addition of no more than 30 amino acids or peptidomimetics to a sequence consisting of SEQ ID NO:1, and that the added sequence does not substantially alter the function of the designated sequence. The Examiner further alleges that the specification lacks guidance as to the length of the polypeptide, and specifically alleges that the specification does not describe why the claimed sequences are an improvement over SEQ ID NO:3 of U.S. Patent No. 5,784,531 (the "'531 patent").

In response, without conceding the correctness of the Examiner's argument but merely to expedite allowance of the claims, applicants have amended claim 1 to recite "An isolated polypeptide consisting of" rather than "An isolated polypeptide consisting essentially of". Accordingly, even if the specification had failed to provide enough guidance as to the length of the polypeptides, which applicants do not concede, the amendment to claim 1 obviates this ground of rejection. With regards to the '531 patent, the enablement requirement of 35 USC 112 1st paragraph does not require that specification detail why the claimed invention is superior to other patented inventions. Therefore, applicants respectfully submit that this argument is not relevant to determining enablement.

(b) The Office Action alleges that page 52 of the specification states that the peptide and compositions claimed by the Applicant can be used to treat patients with PV or to create models of PV. The Office Action further alleges that it is puzzling that a peptide can be used to both induce tolerance and to break tolerance in a patient, lacking an apparent difference in how the peptide would be administered in each case. The Office Action further cites several references to support the conclusion on page 5, first full paragraph, that "it appears that an undue amount of experimentation would be left to a person of skill in the art to use Applicant's claimed invention

based on the lack of working examples, the lack of guidance concerning the use of the same compositions to induce tolerance and induce autoimmunity, and the unpredictability of using peptide-specific compositions to treat diseases in humans."

In response, applicants submit that the pending claims are directed to either an isolated polypeptide (claims 1) or compositions comprising said polypeptide (claims 2-10). The pending claims do not recite methods of inducing tolerance in a patient, methods of breaking tolerance in a patient, or methods of treating pemphigus vulgaris using a peptide consisting of amino acid sequence of SEQ ID NO:1. Accordingly, the extent to which the polypeptides and compositions of the present invention are functional in different clinical applications are irrelevant to the enablement of the pending claims directed to an isolated polypeptide consisting of the amino acid sequence represented by SEQ ID NO: 1 or to compositions thereof. While possibly relevant to determining the utility of a composition under USC 101, such inquiry into the *in vivo* efficacy of the polypeptides in treating a disease are irrelevant to determining the enablement requirement of the pending composition claims.

In addition, the specification provides sufficient description of how the claimed peptides and compositions of the present invention may be useful in immunological settings, further satisfying the enablement requirement. For example, pages 52-56 of the originally-filed specification describes multiple uses of the peptides, including the following:

(i) the use of the peptides to generate animal models of autoimmune disease though immunization with the peptides (page 52, lines 4-10);

(ii) the administration of the peptide at high doses to induce high dose tolerance, with specific reference to WO94/06828 (page 52, line 15 to page 53, line 19);

(iii) the vaccination of a subject against a human pathogen implicated in the etiology of a human autoimmune disease such as pemphigus vulgaris (page 53, line 20 to page 56 line 4).

Finally, with regards to the statement that it is puzzling that a peptide can be used to both induce tolerance and to break tolerance in a patient, applicants submit that it is well-known in the art that allergic reactions can both be caused by an allergen (*i.e.* exposure to the allergen leads to

hypersensitization to the allergen) and treated with high doses of the allergen (*i.e.* high doses of the allergen lead to desensitization to the allergen); see for example (Huggins JL et al. (2004) Allergen immunotherapy. *Am Fam Physician.* 15;70(4):689-96; Norman PS. (2004) Immunotherapy: 1999-2004. *J Allergy Clin Immunol*;113(6):1013-23; Ramirez et al. (2002) Immunotherapy for allergic asthma. *Med Clin North Am.*; 86(5):1091-112). Accordingly, although seemingly paradoxical, one skilled in the art would appreciate that the polypeptides of the present invention may be administered to a patient under different conditions, such as at different dosages, depending on the desired immunological effect on tolerance.

According to MPEP 2164.01, the test of enablement is whether the practice of the invention by one skilled in the art requires undue experimentation. The examples in the instant specification provide such detailed description for the synthesis of the isolated polypeptide of claim 1 that one skilled in the art would not engage in undue experimentation in synthesizing the polypeptide of claim 1. Accordingly, claim 1 and its dependent claims satisfy the enablement requirement.

Should the Examiner maintain the enablement rejection in a subsequent office action, applications respectfully request that the examiner carefully analyze each of the following eight factors:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of no enablement must be based on the evidence as a whole. 858 F.2d at 737, 740, 8 USPQ2d at 1404, 1407."

Based on the arguments set forth above showing compliance with the enablement requirement, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

Claim Rejections under 35 USC 112 1st Paragraph-Written Description

The Office Action rejects claims 1-11 under 35 USC 112 1st paragraph as allegedly failing to comply with the written description requirement. The Office Action alleges that the claims contain subject matter which was not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action alleges that the term "consisting essentially of" encompasses the addition of no more than 30 amino acids or peptidomimetics to a sequence consisting of SEQ ID NO:1, and that the genus of peptidomimetics has substantial variability not disclosed in the subject specification.

In response, applicants note that claim 1, as amended, no longer recites "consisting essentially of" and instead recites the phrase "consisting of." Accordingly, the polypeptide of claim 1 no longer encompasses the addition of amino acids or peptidomimetics to a sequence consisting of SEQ ID NO:1. A polypeptide consisting of the sequence of SEQ ID NO:1, as well as methods for its synthesis, are explicitly described in the specification, thereby complying with the written description requirement. Accordingly, applicants respectfully request reconsideration and withdrawal of this ground of rejection.

CONCLUSIONS

Applicant believes no fee is due with this response. However, if any fee is due, please charge our Deposit Account No. 18-1945, under Order No. PEPT-P01-005 from which the undersigned is authorized to draw.

Dated: February 3, 2005

Respectfully submitted,

By _____

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